

WHAT IS CLAIMED IS:

1. A mutant protein derived from a wild-type human Bcl-2 protein wherein a sequence of amino acid residues comprising a flexible loop from said wild-type human Bcl-2 protein is replaced with a replacement amino acid sequence comprising at least two acidic amino acids.

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2. The mutant protein of Claim 1 wherein said replacement amino acid sequence comprises a sequence of at least a portion of a flexible loop from human Bcl-x_L protein.

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3. The mutant protein of Claim 2 wherein the replacement amino acid sequence comprises the sequence of SEQ ID NO:1.

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4. The mutant protein of Claim 1 wherein the replacement amino acid sequence comprises a sequence of at least 4 to about 50 amino acid residues.

5. The mutant protein of Claim 1 wherein said replacement amino acid sequence comprises a sequence of at least 16 to about 25 amino acid residues.

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6. The mutant protein of Claim 1 wherein said acidic amino acids are glutamic acid.

7. The mutant protein of Claim 1 wherein said acidic amino acids are aspartic acid.

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8. The mutant protein of Claim 1 wherein said acidic amino acids are a glutamic acid and aspartic acid.

9. The mutant protein of Claim 1 wherein said amino acid residues which encode a flexible loop from said human Bcl-2 protein comprise amino acids 35-91 of said human Bcl-2 protein.

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10. The mutant protein of Claim 1 which has an isoelectric point lower than that of wild-type Bcl-2.

11. The mutant protein of Claim 10 wherein said isoelectric point is from 4.5 to about 6.0.

12. The mutant protein of Claim 10 wherein said isoelectric point is from 5.0 to about 5.5.

13. The mutant protein of Claim 10 wherein said isoelectric point is 5.0.

14. A mutant protein having an amino acid sequence comprising:

MAHAGRTGYDNREIVMKYIHYKLSQRGYEWDA~~GDDVEENRT~~EAPEGTESEVVHLA
LRQAGDDFSRRYRGDFAEMSQLHLTPFTARGFATVVEELFRDGVNWGRIVAFFEF
GGVMCVESVNREMSPLVDNIALWMTEYLNRLH~~FT~~WIQDNGGWDAFVELYGPSMR
(SEQ ID NO:2).

15. An assay for identifying substances which bind to a Bcl-2 protein, the assay comprising the steps of:

- (a) providing a candidate substance to be tested;
- (b) providing a labeled peptide which is capable of binding tightly to said mutant protein of Claim 1;
- (c) forming a complex of the labeled peptide with said mutant protein;
- (d) forming a reaction mixture by contacting the candidate substance with the labeled peptide/mutant protein complex;
- (e) incubating the reaction mixture under conditions sufficient to allow the candidate substance to react and displace the labeled peptide; and

(f) determining the amount of labeled peptide that has been displaced from binding to said mutant protein.

16. The assay of Claim 15 wherein the peptide is labeled with radioisotopes, fluorescent
5 moieties, enzymes, specific binding molecules or particles.

17. The assay of Claim 16 wherein the peptide is labeled with a fluorescein compound.

18. The assay of Claim 17 wherein the peptide is labeled with fluorescein isothiocyanate or
5-carboxy-fluorescein.